REMARKS

Request for Withdrawal of Finality

In the Final Rejection set forth in the Office Action of September 11, 2007, the Claims 1, 3-15, and 17-60 are again rejected as allegedly being obvious in view of the abstract by De Bono et al. in combination with Chu et al. (US 5,817,667) and Benet et al. This first time this rejection was presented was in the Office Action of December 19, 2006.

However, as presented in the Office Action of September 11, 2007, the rejection is **not** in view of De Bono et al., Chu et al., and Benet et al. Instead, it is a completely new rejection based on a new combination of prior art, namely De Bono et al., Chu et al., Benet et al., and **the newly applied reference Lokich et al.**

As noted, the first time a rejection in view of view of De Bono et al., Chu et al., and Benet et al. was presented was in the December 19, 2006 Office Action. See pages 11-15 of that Office Action. In that rejection there is absolutely no mention of the reference Lokich et al.

Conversely, in the rejection in view of De Bono et al., Chu et al., and Benet et al. presented in the Office Action of September 11, 2007, the Lokich et al. reference figures prominently. Lokich et al. is discussed in detail at pages 5-7 of the Office Action. Moreover, it is clear that Lokich et al. is being relied on to allegedly overcome a discrepancy in the previous combination of De Bono et al., Chu et al., and Benet et al. regarding the duration of the infusion administration.

At page 18, the Examiner states that the arguments responding to applicants' arguments presented previously in the Office Action (which includes the arguments based on Lokich et al. at page 5-7) are incorporated into the 103 rejection. Furthermore, the 103 rejection expressly cites the Lokich et al, reference with respect to infusion duration (see text bridging pages 19-20 of the Office Action). Furthermore, the rejection again specifically relies on Lokich et al. in making the conclusion of obviousness. See middle of page 4 of the Office Action.

It is noted that the Office Action alleges that applicants' amendment necessitated the new ground of rejection. Firstly, as can be seen from the above, the Office Action does not expressly state a new ground of rejection, but does in fact present one. Secondly, Lokich et al. is relied on

to address a deficiency in the previous prior art rejection, not any new aspect added to the claims by amendment. Finally, the only amendments made to the claims in the Reply filed May 14, 2007, were to dependent claims 4, 18, and 49. These claims were amended to state that the cancer is leukemia selected from a specified group, and applicants pointed out that these amendments did not narrow the scope of the claims, and no new matter was added.

In addition to the 103 rejection, the Office Action presents an obviousness double-patenting rejection in view of Gourdeau (US 6,630,480) in combination with **Gourdeau (US 6,747,036),** Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and the article by De Bono et al. Further, it is evident from the Office Action that this rejection also relies on the disclosure of the newly applied reference, **Lokich et al.** Additionally, this is also a new ground of rejection which was not necessitated by any amendment. A prior similar rejection did not include the references Gourdeau (US 6,747,036) and/or Lokich et al.

Additionally, the Office Action presented a third rejection, i.e., an obviousness double-patenting rejection in view of Serial No. 10/824,563 in combination with **Gourdeau (US 6,630,480), Gourdeau (US 6,747,036),** Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and the article by De Bono et al. Further, it is evident from the Office Action that this rejection also relies on the disclosure of the newly applied reference, **Lokich et al.** Additionally, this is also a new ground of rejection which was not necessitated by any amendment. A prior similar rejection did not include the references Gourdeau (US 6,630,480), Gourdeau (US 6,747,036) and/or Lokich et al.

Thus, all three rejections presented in the Final Office Action are in fact new grounds of rejection, none of which were necessitated by any amendment. In view of the above remarks, withdrawal of the finality of the prior Office Action is respectfully requested.

Obviousness-Type Double Patenting Rejections

In the Office Action, there are two rejections based on grounds of obviousness-type double patenting. Specifically, claims 1, 3-15, and 17-60 are rejected on grounds of obviousness-type double patenting in view of certain claims of Gourdeau (US 6,630,480) in combination with Gourdeau (US 6,747,036), Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and the article

by De Bono et al. As noted above, a prior similar rejection, which was withdrawn, did not include the reference Gourdeau (US 6,747,036).

Additionally, claims 1, 3-15, and 17-60 are rejected on grounds of obviousness-type double patenting in view of certain claims of Serial No. 10/824,563 in combination with Gourdeau (US 6,630,480), Gourdeau (US 6,747,036), Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and the article by De Bono et al. As noted above, prior similar rejection, which was withdrawn, did not include the references Gourdeau (US 6,630,480) and Gourdeau (US 6,747,036).

With respect to the obviousness-type double patenting rejection in view of certain claims of Serial No. 10/824,563, this rejection is rendered moot by the abandonment

As for the rejection in view of certain claims of Gourdeau (US 6,630,480) in combination with Gourdeau (US 6,747,036), Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and the article by De Bono et al., this rejection should be withdrawn for at least the same reasons that the prior rejection based on the combination of Gourdeau (US 6,630,480) Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and De Bono et al. was withdrawn.

In the Office Action at pages 2-3, the Examiner sets forth five points which are asserted to be contentions from applicants' Reply filed May 14, 2007 (applicants are not agreeing that these with the only arguments made in the May 14, 2007 Reply) . With respect to the first three contentions, the Examiner specifically states that:

"Applicant's arguments identified under items #1-3 are found to be persuasive. The Rejections based on said references are withdrawn."

The Examiner characterizes argument #3 at the top of page 3 of the Office Action as follows:

"Gourdeau '480 is not effective prior art for obviousness determinations under 35

USC 103(a) because it is a divisional of Gourdeau '036 and both Gourdeau '480 and Gourdeau '036 were commonly assigned at the time of the invention of the instant application was made. Also, Gourdeau '639 is ineffective prior art for the same reason because it was also commonly assigned at the time of the invention of the instant application was made."

Compare applicants' May 14, 2007 Reply at the top of page 13. It is noted that there is an obvious typographical error in applicants' arguments, one which is carried over by the Examiner. The paragraph at the top of page 13 of the Reply should have stated that **Gourdeau '036** was not effective art for obviousness determinations under 35 USC 103(a) and the Examiner presents no authority to suggest that **Gourdeau '036** can be used as a secondary reference in an obviousness-type double patenting rejection. It is noted that Gourdeau '036, not Gourdeau '480, is a secondary reference in the relevant obviousness-type double patenting rejection.

In any event, the Examiner agreed that Gourdeau '639 could not be used as a secondary reference in an obviousness-type double patenting rejection. Since the present rejection employs Gourdeau '639 in exactly that capacity, the rejection should be withdrawn based on the same arguments that the Examiner has already agreed were persuasive.

To summarize again the relative relationships of the Gourdeau references, the secondary reference Gourdeau et al. (US '036) is a divisional of the primary reference Gourdeau et al. (US '480). The instant application, as well as Gourdeau et al. (US '036), are commonly assigned. Additionally, the instant application and the secondary Gourdeau et al. (US '639) are also commonly assigned, and were commonly assigned at the time the invention of the instant application was made.

Thus, neither Gourdeau et al. (US '036) nor Gourdeau et al. (US '639) are effective prior art for obviousness determinations under 35 USC 103(a). The Examiner cites no authority that suggests that, if secondary reference is not prior art for obviousness determinations under 35

USC 103(a), it can still be used as a secondary reference in an obviousness-type double patenting rejection.

In addition, the applicants maintain that the rejection should also be withdrawn in view of the other arguments presented in the May 14, 2007 Reply.

In view of the above remarks, it is respectfully submitted that the claims of Gourdeau (US 6,630,480), taken alone or in combination with the disclosures of (US 6,747,036), Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and/or the article by De Bono et al., fail to render obvious applicants' claimed invention. Further, the rejection in view of Serial No. 10/824,563 in combination with Gourdeau (US 6,630,480), Gourdeau (US 6,747,036), Gourdeau (US 6,800,639), Chu et al. (US 5,817,667), and the article by De Bono et al. is rendered moot by the abandonment of Serial No. 10/824,563. Withdrawal of the rejections is respectfully requested.

Rejection under 35 USC §103(a)

Claims 1, 3-15, and 17-60 are rejected as allegedly being obvious in view of the abstract by De Bono et al. in combination with Chu et al. (US 5,817,667) and Benet et al. This rejection is respectfully traversed.

The rejection is traversed for at least the same reasons presented in applicants Reply of May 14, 2007, which arguments are hereby incorporated in this response.

At page 4 of the September 17, 2007 Office Action, the Examiner asserts that applicants' "conclusory statement" regarding lack of teaching or suggestion in the prior art was not persuasive. Applicants did not make such conclusory statements but instead clearly demonstrated that the prior art did not render obvious the recited claim features regarding continuous infusion.

Further, at page 4 of the September 17, 2007 Office Action, the Examiner asserts that

applicants arguments attacked the references individually, rather than the combination. This also is incorrect. Applicants' arguments demonstrated that as a whole none of the cited prior art references render obvious the recited claim features regarding continuous infusion.

To address applicants' arguments regarding continuous infusion, the Examiner relies on a newly applied reference, Lokich et al. However, taking all of the references together including Lokich et al., the combined prior art does not render obvious applicants' claimed invention.

Lokich et al. describe the results of a literature survey analyzing the relative dose intensity (DI) and maximum tolerated dose (MTD) for bolus versus infusional administration techniques for 27 anti-neoplastic agents. It is noted that troxacitabine is not one of the 27 anti-neoplastic agents included in the analysis.

As shown in Table 6 in the Discussion section at page 22, the majority of the agents fell into a category in which MTD and/or DI were relatively comparable for infusion and bolus administration (dose ratio 1 to5). For certain agents (dose ratio $\leq$ 1), the infusion schedule provided a higher MTD, whereas for other agents with (dose ratios 5-10 and 10-20), it was the bolus schedule that provided a "dramatically higher MTD." Further, with respect to the latter group Lokich et al. note that "the antimetabolites are the only drugs represented."

One of the antimetabolite drugs included in the survey was Ara C. This drug was placed in the highest drug ratio column in Table 6, indicating a dramatically higher MTD for bolus administration. It is noted that Ara C is a nucleoside analogue. This would lead one of ordinary skill in the art to believe that similar results would be expected for other nucleoside analogues, like troxacitabine.

Alternatively or additionally, one of ordinary skill in the art may not have any expectation as to the optimal methodology for administering troxacitabine. Unlike Ara-C and other nucleoside analogues used as anti-neoplastic agents, troxacitabine was the first unnatural L-

nucleoside analog to show potent preclinical anti-tumor activity, thus effecting representing a new class of agents.

Furthermore, clinical trial results for troxacitabine pointed away form administration of the drug by continuous infusion for a period of at least 72 hours for achieving a steady state plasma or maximum plasma concentration of 0.03 to 2.0 μM. See the page 2, lines 19-34 of applicants' specification.

Thus, it is respectfully submitted that, upon consideration of all of the factors discussed above, one of ordinary skill in the art would not have consider applicants' claimed method to be obvious.

In view of the above remarks, it is respectfully submitted that De Bono et al., taken alone or in combination with US '667 and/or Benet et al. and/or Lokich et al., fails to render obvious applicants' claimed invention. Withdrawal of the rejection is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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